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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/624,530	07/24/2000	Richard Sackler	200.93185C2C	5659

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	**PAPER NUMBER**
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/624,530	SACKLER ET AL.	
	Examiner	Art Unit	
	YONG S. CHONG	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-8, 13-16, 24-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-8, 13-16, 24-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 12/15/08.

Claim(s) 1-5, 9-12, 17-23 have been cancelled. Claim(s) 39-43 have been added.

Claim(s) 6-8, 13-16, 24-43 are pending. Claim(s) 6, 24, 35, 37 have been amended.

Claim(s) 6-8, 13-16, 24-43 are examined herein.

Applicant's claim amendments have rendered the 103(a) rejection of the last Office Action moot, therefore hereby withdrawn. The following new rejection will now apply.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 6-8, 13, 24-38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 5,958,459. Although the conflicting claims are not identical, they are not

patentably distinct from each other because the pending claims are drawn to a method of treating pain comprising administering a composition comprising hydromorphone coated with a hydrophobic polymer having peak plasma concentration from about 4 to 6 hours, whereas the referenced claims are drawn to a composition comprising an opioid analgesic, hydromorphone, coated with a hydrophobic polymer having peak plasma concentration from about 4 to 6 hours. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating pain with such composition since the main active agents is disclosed to be an opioid analgesic, which is a well known agent to treat pain in humans.

Claims 6-8, 13, 24-38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,143,322. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims are an obvious variation of each other since both disclose a method of treating pain comprising administering a composition comprising hydromorphone coated with a hydrophobic polymer having peak plasma concentration from about 4 to 6 hours. It is noted that the same arguments regarding the limitations of the dissolution profile as well as the C_{max} and C_{24} values are also applied here.

Response to Arguments

Applicant has not addressed the double patenting rejections at this time.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 6-8, 13-16, 24-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldie et al. (US Patent 4,844,909) in view of Oshlack et al. (US Patent 5,286,493).

Goldie et al. teaches a solid release oral dosage form, the dosage form for the treatment of moderate to severe pain (col. 1) comprising a therapeutically effective amount of hydromorphone or salt thereof in a matrix wherein the dissolution rate in vitro of the dosage form, when measured by the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm at 900 mL aqueous buffer at pH 1.6 and 7.2 and at 37 °C overlaps with those as instantly claimed (Abstract). Peak plasma level is achieved between 2 and 4 hours (Abstract). The amount of hydromorphone released at a pH of

1.6 is less than 10% than that released at any pH up to 7.2 (col. 1, lines 29-35). Therapeutic levels of hydromorphone are maintained in vivo for *at least* 12 hours (col. 2, lines 3-10). Compositions wherein peak plasma levels are achieved between 4 and 8 hours are also taught to provide at least 12 hours of therapeutic effect (col. 2, lines 11-23). Gums, cellulose ethers, acrylic resins, C8-C50 long chain hydrocarbons, fatty acids, fatty alcohols, mineral oils, vegetable oils, waxes and polyalkylene glycols are disclosed as matrix materials (col. 2, line 47-col. 3, line 6). Dosage forms comprising between 2 and 40 mg of hydromorphone are taught (col. 2, lines 41-46). Blood plasma levels are exemplified as 1.0 ng/mL and 2.1 ng/mL at 12 hours and 1.1 ng/mL and 1.4 ng/mL at 24 hours (Tables 5 and 6). Goldie et al. also teach a dosage form comprising film-coated spheroids. The spheroids may contain water insoluble polymers, such as acrylic polymer and ethyl cellulose. The spheroids are film coated with a material that permits release of the active agent in a controlled rate. The film coat includes a water insoluble polymer, such as ethyl cellulose (col. 3, line 66 to col. 4, line 59). The examples also show that the coating is cured by way of exposure to heat of up to 50 and 60 °C.

Examiner notes that the limitations regarding "a dissolution profile which is substantially unaffected by exposure to storage conditions of at least a month at a temperature of 40 °C and a relative humidity of 75%" as well as C_{max} and C_{24} values are inherent when the same composition is cited by the prior art at the same dosage.

"Products of identical chemical composition can not have mutual exclusive properties." Any properties exhibited by or benefits from are not given any patentable

weight over the prior art provided the composition is inherent. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the disclosed properties are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The burden is shifted to the applicant to show that the prior art product does not inherently possess the same properties as the instantly claimed product.

It would have been obvious to one of ordinary skill in the art at the time of the invention to prepare a dosage form wherein the peak plasma level is obtained between 4.4 and 8 hours, 4.6 and 8 hours, 4.8 and 8 hours, or 5.5 and 8 hours after administration of the dosage form because it is well known in the pharmaceutical art to have produced a formulation that gives a peak plasma level of the drug between 4 to 8 hours after administration. One would have been motivated to prepare a dosage form, which achieved maximum plasma levels between 4.4 to 8 hours to 5.5 to 8 hours because of an expectation of similar success in preparing a dosage form, which achieved therapeutic effects for at least 12 hours. Furthermore, even if between 2 and 4 hours is not considered inclusive of 4 hours, it would have been obvious to one of ordinary skill in the art at the time of the invention to utilize a dosage form with a the peak plasma level obtained between 4 and 8 hours after administration of the dosage form because Goldie et al. teaches that dosage forms achieving a peak plasma level between 2 and 4 hours are, surprisingly, interchangeable with dosage forms that achieve peak plasma levels between about 4 and 8 hours after administration. Both dosage forms are taught to achieve the desired effect. Namely, both are taught to

achieve a therapeutic effect for at least 12 hours. Accordingly, one would have been motivated to administer a dosage form that achieves a peak plasma level between 4 and 8 hours after administration because of an expectation of administering a dosage form suitable for achieving a therapeutic effect for at least 12 hours. It is noted that the exemplified clinical studies teach plasma levels at 24 hours wherein the amount present is a therapeutically effective amount because (1) the dosage form is taught to be therapeutically effective for at least 12 hours and the plasma levels at 24 hours are not significantly different than the plasma levels at 12 hours; and (2) the plasma levels are within the scope of the plasma levels as instantly claimed.

Goldie et al. teach as discussed above, however fail to specifically disclose a coating that has been stabilized by curing for about 24 hours or more at a temperature greater than the glass transition temperature of the hydrophobic polymer and at a relative humidity from about 60 to 100%.

Oshlack et al. teach that prior art curing of hydromorphone formulations have stability problems with respect to the controlled release dissolution profile (example 4). Oshlack et al. solves this problem by introducing a new method for obtaining a stabilized controlled release formulation by preparing a solid substrate comprising a therapeutically active agent, such as hydromorphone (col. 7, line 32), overcoating said substrate with a sufficient amount of a plasticized aqueous dispersion of an acrylic polymer, and then curing the coating substrate at a temperature above the glass transition temperature of the plasticized acrylic polymer, until the coated dosage form attains a stabilized dissolution profile substantially unaffected by exposure to storage

conditions of elevated temperature and/or elevated relative humidity (abstract and claims). Generally the curing time is about 24 hours or more (col. 8, lines 55-56). Furthermore, Oshlack et al. also teach that the substrate is overcoated with a barrier agent, to separate the therapeutically active agent from the acrylic coating (col. 7, lines 56-60).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have used the coating and curing process as taught by Oshlack et al. in the process of formulating the controlled release oral dosage formulation comprising hydromorphone for the method of treating pain as taught by Goldie et al.

One would have been motivated to use the coating curing process as taught by Oshlack et al. in the process of formulating the controlled release oral dosage formulation comprising hydromorphone for the method of treating pain as taught by Goldie et al. because: (1) both Oshlack and Goldie et al. teach controlled release oral dosage formulations comprising hydromorphone; (2) both Oshlack and Goldie et al. teach coatings that are cured; (3) Oshlack et al. teach that traditional curing has stability problems associated with the dissolution profile; (4) Oshlack et al. teach method of overcoming these stability problems by curing the coating substrate at a temperature above the glass transition temperature for over 24 hours, which provides a stabilized dissolution profile substantially unaffected by exposure to storage conditions of elevated temperature and/or elevated relative humidity. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in formulating a stabilized controlled release oral dosage form comprising hydromorphone, which possesses a

stabilized dissolution profile substantially unaffected by exposure to storage conditions of elevated temperature and/or elevated relative humidity.

Response to Arguments

Applicant arguments directed to the new claim limitations regarding curing, dissolution profile, and barrier coating have been addressed in the new obviousness rejection above.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/YONG S. CHONG/
Primary Examiner, Art Unit 1617

YSC